CPMA

COLOR PIGMENTS MANUFACTURERS ASSOCIATION, INC.

201-16302

August 1, 2006

Mr. Jeffrey Taylor
U.S. Environmental Protection Agency
EPA East Building
Room 4410H (MC7405)
1200 Pennsylvania Ave, NW
Washington, DC 20004
202.564.8828

Dear Mr. Taylor:

On June 9, 2006 CPMA submitted to you six test plans prepared by committees of the Color Pigments Manufacturers Association, Inc. (CPMA) under EPA's High Production Volume Chemical Testing Program:

- Test Plan for 6-Amino-4-chloro-m-toluenesulfonic acid (2B Acid) and 2-Amino-5-chloro-ptoluenesulfonic acid (C Amine),
- Test Plan 3,3' Dichlorobenzidine Dihydrochloride,
- Test Plan for C. I. Pigments Violet 19, Red 122, and Dihydro Quinacridone,
- Test Plan for C. I. Pigment Red 48 (Barium), C.I. Pigment Red 48 (Calcium) and C.I. Pigment Red 52 (Calcium),
- Test Plan for C.I. Pigment Yellow 14, and
- Test Plan for C. I. Pigment Red 49 (Barium)

The test plans were formatted incorrectly and were actually earlier drafts. As a result, we are submitting the revised test plans.

Two test plans have already been posted on the EPA web site: Test Plan for C. I. Pigment Red 49 (Barium) and Test Plan for C6-Amino-4-chloro-m-toluenesulfonic acid (2B Acid) and 2-Amino-5-chloro-ptoluenesulfonic acid (C Amine). Your removal of these two tests plans from the site and replacing them with the enclosed revised test plans is appreciated.

The remaining test plans that were previously sent and have not yet been posted should be disregarded, and replaced with the corrected versions.

Thank you for your attention to this.

Sincerely,

J. Lawrence Robinson
President

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Mailing Address: P.O. Box 20839 • Alexandria, Virginia 22320-1839 • e-mail: cpma@cpma.com

August 8, 2006

Dear NCIC,

Please replace the previous 6 CPMA test plan and robust summary submissions (AR201-16298 through AR201-16303) from June 2006 with these newly corrected 6 CPMA test plan and robust summary submissions. CPMA phoned me to say that no substantial information was changed; only the formatting was corrected. Please give these new submissions the same AR numbers that you had previously used for them, and also process this cover page of mine along with CPMA's new cover page that they have attached to the new materials.

Thank you,
Jeffrey Taylor

Jeffrey A. Taylor
U.S. Environmental Protection Agency
Office of Pollution Prevention and Toxics
Chemical Control Division
EPA East -- Room 4410-H, Mail Code 7405M
1200 Penn Ave NW, Washington. DC 20004
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201-16302

HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

TEST PLAN
FOR

C.I. Pigment Red 48 (Calcium)
(CAS NO.: 7023612)
and
C.I. Pigment Red 48 (Barium)
(CAS NO.: 7585413)

and
C.I. Pigment Red 52 (Calcium)
(CAS NO.: 17852992)

PREPARED BY:
COLOR PIGMENT MANUFACTURERS ASSOCIATION, INC.
MONOAZO AND RELATED PIGMENTS COMMITTEE

June, 2006

TABLE OF CONTENTS

OVERVIEW

The Monoazo and Related Pigments Committee ("MRPC") of the Color Pigment Manufacturers Association, Inc. (CPMA) and its member companies hereby submits for review and public comment the test plan for C.I. Pigment Red 48 (Calcium) (CAS NO.: 7023612) and C.I. Pigment Red 48 (Barium) CAS NO.: 7585413) under the Environmental Protection Agency's (EPA) voluntary High Production Volume (HPV) Challenge Program. It is the intent of the MRPC and its member companies to use existing data, and predictive computer models to adequately fulfill the Screening Information Data Set (SIDS) for the various physicochemical, environmental fate, ecotoxicity test, and human health effects endpoints.

C.I. Pigment Red 48 (Calcium) (CAS NO.: 7023612) , C.I. Pigment Red 48 (Barium) (CAS NO.: 7585413) and C.I. Pigment Red 52 (Calcium) (CAS NO.: 17852992) are stable solids. These chemicals are used to provide color for the printing inks, paints and plastics industries. These chemical are stable and is considered "not readily biodegradable".

TEST PLAN SUMMARY

CAS No.7023612, 7585413 and 17852992	Information Y/N	OECD Study Y/N	Other Y/N	Estimation Y/N	GLP Y/N	Acceptable Y/N	New Testing Req. Y/N
PHYSICAL CHEMICAL DATA							
Melting Point	Y	-	-	Y	N	Y	N
Boiling Point	N/A	-	-	Y	N	Y	N
Vapor Pressure	Y	-	-	Y	N	Y	N
Partition Coefficient	Y	-	-	Y	N	Y	N
Water Solubility	Y	Y	-	Y	Y	Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	N	-	Y	N	Y	N
Stability in Water	N\A	Y			Y	Y	N
Biodegradation	Y	Y	Y	-	Y	Y	N
Transport between Environmental Compartments	Y	Y	-	Y	N	Y	N
(Fugacity)	Y			Y		Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	Y	-	-	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y		-	Y	Y	N
Toxicity to Aquatic Plants	Y	Y		-		Y	N
TOXICOLOGICAL DATA							
Acute Toxicity	Y	Y	Y	-	Y	Y	N
Repeated Dose Toxicity	Y	Y		-	Y	Y	N
Genetic Toxicity – Mutation	Y	Y	Y	-	Y	Y	N
Genetic Toxicity – Chromosomal Aberrations	Y	Y	Y	-	Y	Y	N
Developmental Toxicity	Y	Y		-	Y	Y	N
Toxicity to Reproduction	Y	Y		-	Y	Y	N

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physicochemical

Melting point - A value for this endpoint was obtained from a reputable journal and through surrogate data

for C.I. Pigment Red 57

Boiling Point - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.

Vapor Pressure - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN.

Partition Coefficient - A value for this endpoint was obtained from analysis of a surrogate substance C.I. Pigment Red 57

Water Solubility - A value for this endpoint was obtained using a computer estimation-modeling program within EPIWIN. A value for this endpoint was also obtained from analysis of a surrogate substance C.I. Pigment Red 57

Conclusion: All end points have been satisfied by utilizing data obtained from the various physical chemical data modeling programs within EPIWIN or using measured values. The results of the various computer estimation models within EPIWIN have been noted by the Agency as acceptable in lieu of actual data or values identified from textbooks. No new testing is required.

B. Environmental Fate

Photodegradation - A value for this endpoint was obtained using AOPWIN, a computer estimation-modeling program within EPIWIN (1) and through the use of surrogate data for C.I. Pigment Red 57.

Stability in Water - A value for this endpoint was obtained from analysis of a surrogate substance C.I. Pigment Red 57

Biodegradation - This endpoint was satisfied through the use of an OECD-301C test. The study was

Fugacity - A value for this endpoint was obtained using the EQC Level III partitioning computer estimation model within EPIWIN.

Conclusion: All endpoints have been filled with data utilizing acceptable methodologies and of sufficient quality to fulfill these endpoints. No new studies are being proposed.

C. Ecotoxicity Data

Acute Toxicity to Fish-- This endpoint is filled by data from a study that followed OECD TG-203 and was conducted under GLP assurances for the surrogate substance C.I. Pigment Red 57.

Acute Toxicity to Aquatic Invertebrates - This endpoint is filled by data from a study that followed OECD TG-202 and was conducted under GLP assurances for the surrogate substance C.I. Pigment Red 57.

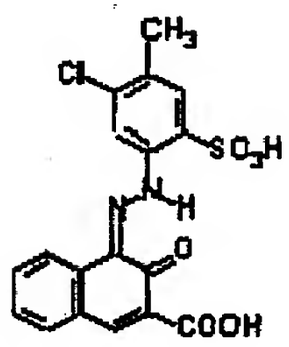
Toxicity to Aquatic	This endpoint is filled by data from a study that followed OECD TG-201 for the Plants
Bioaccumulation	This endpoint is filled by data from a GLP study for the surrogate substance C.I. Pigment Red 57.
Conclusion:	All endpoints have been satisfied with data from studies that were conducted using established OECD guidelines. In total, these currently available studies are of sufficient quality to conclude that no additional testing is needed.
D. Toxicological Data Acute Toxicity -	This endpoint is filled by oral exposure data from various published and unpublished references to studies completed in 1961, 1968, 1972, 1976, 1985 and 1992 precise information on protocols followed is not readily available. Nevertheless, given the number of studies and the consistent results, this data is considered "reliable with restrictions". Data for Skin sensitization, skin irritation and eye irritation are also available.
Repeat Dose Toxicity -	This endpoint is filled by data from a study that followed OECD TG-422 for the surrogate substance C.I. Pigment Red 57.
Genetic Toxicity Mutation -	This endpoint is filled by published values supplied by manufacturers and data from a study that followed OECD TG-471 and 472 for the surrogate substance C.I. Pigment Red 57.
Aberration -	This end point is filled by published values supplied by manufacturers and data from a study that followed OECD TG-473 for the surrogate substance C.I. Pigment Red 57.
Developmental Toxicity -	This endpoint is filled by data from a study that followed OECD TG-422 for the surrogate substance C.I. Pigment Red 57.
Reproductive Toxicity -	This endpoint is filled by data from a study that followed OECD TG-422 for the surrogate substance C.I. Pigment Red 57.
Conclusion:	All endpoints have been satisfied with data on C.I. Pigment Red 48 and C.I. Pigment Red 52 or through the use of structural surrogates, primarily C.I. Pigment red 57 which are of sufficient quality to conclude that no additional testing is needed.

Rationalization for Use of Surrogate Data

As a means of reducing the number of tests that may be conducted, the EPA allows for the use of data from structurally similar compounds to characterize specific SIDS endpoints (US EPA 1999a). Accordingly, the MRPC believes that data from the available studies for D & C Red Number 7, C.I. Pigment Red 57 (CAS No. 5281-04-9) meets the needed criteria for use as a surrogate in the completion of some SIDS endpoints. All three color pigments, C.I. Pigment Red 48 and C.I. Pigment Red 57 are derived from beta-oxynaphthoic acid. As is readily seen by their structures below, C.I. Pigment Red 48 Calcium, C.I. Pigment Red 48, Barium, C.I. Pigment Red 52, Calcium and C.I. Pigment Red 57 only differ by the presence of a single chlorine atom and in the case of C.I. Pigment Red 48:1 the use of barium as the metal salt which is used to form the insoluble color pigment instead of calcium. This modification does not significantly alter the basic physicochemical properties or the basic biological effects. All three compounds are almost completely insoluble in water and have similar toxicity and physical properties. The presence of chlorine in C.I. Pigment Red 48 and C.I. Pigment Red 52 increases insolubility, stability and lowers bioavailability. Accordingly, available high quality information developed for C.I. Pigment Red 57 have been used to fulfill a number of the SIDS endpoints.

Common Name: C.I. Pigment Red 48 Calcium

Structure:

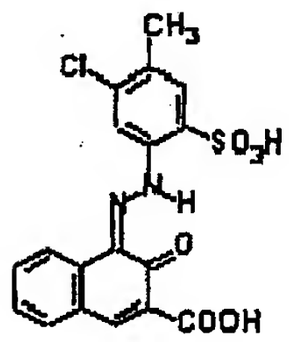


Chemical Name: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl) azo]-, Calcium salt

Melting Point: 360 (measured using the manganese salt, C.I. Pigment Red 48:4, NPIRI 2000)
Boiling Point: Solid
Density 12.5 to 15.5 Pounds Per U.S. Gallon, NPIRI
Acute Toxicity: LD50>5000 mg/kg, NPIRI

Common Name C.I. Pigment Red 48 Barium

Structure:

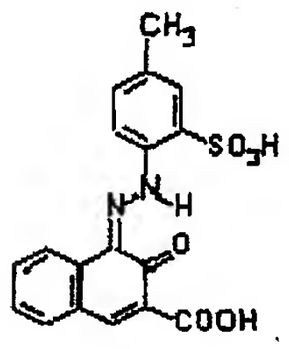


Chemical Name 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Barium salt

Melting Point 360 (measured using the manganese salt, C.I. Pigment Red 48:4, NPIRI 2000)
Boiling Point: Solid
Density 12.4 to 17.4 Pounds Per U.S. Gallon, NPIRI
Acute Toxicity: LD50>5000 mg/kg, NPIRI

Common Name C.I. Pigment Red 57

Structure

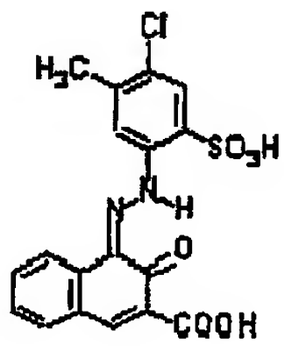


Chemical Name 2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4-methyl-2-sulfophenyl)azo]-, calcium salt

Melting Point 360 NPIRI\ 357.5 °C
Boiling Point: Solid
Density 11.8 to 15.9 Pounds Per U.S. Gallon
Acute Toxicity: LD50>5000 mg/kg, NPIRI, OECD TG 401 LD50 > 5,000 mg/kg
Water Solubility : OECD TG 105 8.9 mg/l at 25 °C

Common Name: C.I. Pigment Red 52 Calcium,

Structure:



Chemical Name: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(4-chloro-5- methyl-2-sulfophenyl)azo]-, Calcium salt

Melting Point: 360 (measured using the manganese salt, C.I. Pigment Red 48:4, NPIRI 2000)
Boiling Point: Solid
Density 11.6 to 14.6 Pounds Per U.S. Gallon, NPIRI
Acute Toxicity: LD50>5000 mg/kg, NPIRI

SIDS DATA SUMMARY

Physical Chemical Endpoints

Data assessing the various physicochemical properties (melting point, boiling point, vapor pressure, partition coefficient, and water solubility) for C.I. Pigment Red 48 Calcium and C.I. Pigment Red 48 Barium, C.I. Pigment Red 52 calcium were also obtained from estimations using the models within EPIWIN. These data indicate that these substances are stable solids at room temperature, are largely insoluble in octanol and is also insoluble in water .

Environment

For the environment, analysis of Pigment Red 57 indicates that: various NOEC and LC50 values were gained from test results; LC50 = 33 mg/l (acute fish); EC50 = 280 mg/l (acute daphnia); EC50 = 190 mg/l (acute algae); NOEC = 3.0 mg/l (long-term daphnia reproduction). Therefore, the chemical is considered to be slightly toxic to fish. The lowest chronic toxicity result for daphnids [21d-NOEC (reproduction) of *Daphnia magna* (3.0 mg/l)] was used with an assessment factor of 100 to determine the PNEC according to the OECD Provisional Guidance for Initial Assessment of Aquatic Effects. Thus, the PNEC of the chemical is 0.03 mg/l in the present report. The PEC is lower than the PNEC, therefore the environmental risk is low.

Acute Toxicity

The potential to induce toxicity in mammalian species following acute oral exposure is very low. All types of Pigment Red 48 and C.I. Pigment Red 57 exhibited LD_{50} values of >5,000 mg/kg.

Human Health

Analysis of C.I. Pigment Red 57 indicated that, the chemical showed no genotoxic effects in bacteria and chromosomal aberration tests *in vitro*. In a combined repeat dose and reproductive/developmental toxicity screening test, increases of kidney weights and decreases of thymus weights were observed in parental animals at the highest dose (1000 mg/kg/day). At the terminal necropsy, gross changes included a small thymus up to the lowest dose (100 mg/kg/day). In the histopathological examinations, regenerated renal tubular epitheliums were also seen at the middle dose (300 mg/kg/day) and at the highest. Regarding reproductive/developmental end-points, there were no effects observed related to mating, fertility and the oestrus cycle and there were no effects observed in dams during the pregnancy and lactation period. Therefore, the NOEL was less than 100 mg/kg/day for repeated dose toxicity and equal to 1000 mg/kg/day for reproductive toxicity. An unpublished chronic toxicity study is known to exist for C.I. Pigment Red 57. This study has been used in support of international approvals for drug and cosmetic colorants and is known to indicate no toxicologically significant results.

Conclusion

All endpoints have been satisfied with data, on C. I. Pigment Red 48 and C.I. Pigment Red 52 or through the use of structural surrogates, which are of sufficient quality to conclude that no additional testing is needed. Since these substances are extremely stable and insoluble in water, ink formulations or other uses such as paints and plastic formulations, and since these substances are encapsulated in these applications, exposure to these products in use is limited.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general US EPA guidance (3) and the systematic approach described by Klimisch *et al.* (4). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to ecotoxicology and human health endpoint studies per EPA recommendation (5). The codification described by Klimisch specifies four categories of reliability for describing data adequacy. These are:

1. Reliable without Restriction: Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.

2. Reliable with Restrictions: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.

3. Not Reliable: Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.

4. Not Assignable: Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in abstracts or secondary literature.

REFERENCES

1. EPIWIN, Version 3.10, Syracuse Research Corporation, Syracuse, New York.

2. US EPA. (1999). The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program. OPPT, EPA.

3. USEPA (1998). 3.4 Guidance for Meeting the SIDS Requirements (The SIDS Guide). Guidance for the HPV Challenge Program. Dated 11/2/98.

4. Klimisch, H.-J., Andreae, M., and Tillmann, U. (1997). A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Regul. Toxicol. Pharmacol.* 25:1-5.

5. USEPA. 1999. Determining the Adequacy of Existing Data. Guidance for the HPV Challenge Program. Draft dated 2/10/99.

I. General Information

CAS Number:	C.I. Pigment Red 48 (Calcium), CAS NO.: 7023612
Name:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, calcium salt
CAS Number:	C.I. Pigment Red 48 (Barium), CAS NO.: 7585413
Name:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, barium salt
CAS Number:	C.I. Pigment Red 52 (Calcium), CAS NO.:17852992
Name:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-(4-chloro-5- methyl-2-sulfophenyl)azo]-, Calcium salt

II. Physical-Chemical Data

A1. Melting Point

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Manganese salt
Remarks:	

Method

Method:	Measured
Remarks:	Mean of the Joback, and the Gold and Ogle methods

Results

Melting point value:	360 °C
Remarks:	

References National Printing Ink Research Institute, Raw Materials Handbook, 2000

Other

Data is consistent with melting points for the class of pigments and other available measurements

A2. Melting Point

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt

Remarks:

Method

Method: Measured

Remarks:

Results

Melting point value: 357.5 °C

Remarks:

References

Unpublished company data
reliable with restrictions

Other

Data is consistent with melting points for the class of pigments and other available measurements.

B. Boiling Point

Test Substance

Test substance: SOLID

Remarks:

Method

Method:

Remarks:

Results

Boiling point value:

Remarks:

References

Other

C1. Vapor Pressure

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4- (5-chloro-4- methyl-2-sulfophenyl)azo]-, Calcium salt

Remarks:

Method

Method: Estimation

Remarks: Modified Grain method

Results

Vapor pressure value: 2.9 E-019 mm Hg

Temperature:

Remarks:

References

MPBPWIN v 1.40 in EPIWIN v 3.10, Syracuse Research Corporation, Syracuse, New York

Other

C2. Vapor Pressure

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt

Remarks:

Method

Method: OECD TG104,

Remarks:

Results

Vapor pressure value: <130 PA

Temperature: 25 °C

Remarks:

References

Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1993)

Other

D. Partition Coefficient

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt

Remarks:

Method

Method: Measured Value, OECD 117

Remarks: GLP

Results

Log P_{OW}: -2.5 at pH 3, 2.4 at pH 4, 1.1 at pH 7

Remarks:

References

Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1993)

Other

E. Water Solubility

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt
Remarks:	

Method

Method:	Measured Value OECD 105
Remarks:	GLP

Results

Value:	8.9 mg/L
Temperature:	25 °C
Description:	Very Low Solubility
Remarks:	

References

Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1993)

Other

III. Environmental Fate Endpoints

A. Photodegradation

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt

Remarks:

Method

Method: Estimate

Test type: Water\sunlight

Remarks:

Results

Temperature:

Degradation Rate

2.25 x 10-11 mol/l/s

: Half-life

Ozone reaction: .049 yearsNo ozone reaction estimation

Remarks:

Conclusions

References

Lyman, W. J., W. F. Reehl and D. H. Rosenblatt (1981) "Handbook of Chemical Property Estimation Method", McGraw Hill Book Co.

Other

A2. Photodegradation

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4- (5-chloro-4- methyl-2-sulfophenyl)azo]-, Calcium salt

Remarks:

Method

Method: Estimation
Test type: Water
Remarks:

Results

Temperature:
Hydroxyl radicals reaction
OH Rate constant:
Half-life 1.56 E6OH/cm3
Ozone reaction: .957 Days
Remarks:

Conclusions

References

AopWin v1.90 in EPIWIN v3.10, Syracuse Research Corporation, Syracuse, New York

Other

B. Stability in Water

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt
Remarks:	

Method

Method:	OECD Test 111
Test type:	abiotic hydrolysis
GLP:	Yes
Remarks:	

Results

Half-life:	not hydrolyzed at pH 4, 7 and 9
Percent hydrolyzed in 5 days (120 hs) at 50 °C :	
Remarks:	

Conclusions

Data Quality

Remarks:	Reliable without Restriction

References Ministry of Health and Welfare (MHW), Ministry of International Trade and Industry (MITI)

Other Environment Agency (EA), Japan (1993)

C. Biodegradation

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt

Remarks:

Method

Method: OECD 301C

Test type: Biological Oxygen Demand (BOD)
GLP: Yes
Year: 1993
Remarks: Degree of degradation after 28 days (Japanese standard activated sludge)

Results

Results: 12.9 and 9 percent from BOD
Remarks:

Conclusions

Data Quality

Remarks: This was a well-documented study that followed established guidelines and was conducted under GLP assurances.

References

Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1992)

Other

D. Transport between Environmental Compartments (Fugacity)

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4- (5-chloro-4- methyl-2-sulfophenyl)azo]-, Calcium salt

Remarks:

Method

Test type: Estimation

Model used: Level III Fugacity Model; EPIWIN:EQC from Syracuse Research Corporation

Remarks:

Results

Model data and results:

Distribution (%)	
Air	.0424
Water	1.17
Soil	51.9
Sediment	46.9

Remarks: Since no experimental values were available the physical chemical values utilized in this model were default parameters from within EPIWIN.

Conclusions

References

Meylan, W. (1993). User's Guide for the Estimation Programs Interface (EPI), Version 3.10, Syracuse Research Corporation, Syracuse, New York 13210. The Level III model incorporated into EPIWIN is a Syracuse Research Corporation adaptation of the methodology described by Mackay *et al.* 1996; *Environ. Toxicol. Chem.* **15(9)**, 1618-1626 and 1627-1637.

Other

IV. Ecotoxicity

A. Acute Toxicity to Fish

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt
Remarks:	Purity was 87.1%

Method

Method:	OECD 203
Test type:	Flow through
GLP:	No
Year:	1992
Species/strain:	Oryzias latipes (Orange Killifish)
Analytical monitoring:	No; Exposure solutions, temperature, pH, dissolved oxygen
Exposure period:	96-Hour
Remarks:	A group of 10 fishes were exposed to 5 nominal concentrations(17.1-180), DMSO Control(.5mg/l)and laboratory water control

Results

Nominal concentration:	
Measured concentration:	
Endpoint value:	96-hour LC_{50} 33 mg/L, 72-hour LC_{50} 44mg/L, 48 hour LC_{50} 80-120 mg/L
Biological observations:	
Statistical methods:	
Remarks:	

Conclusions Reliable with restrictions, This appears to be a well documented study.

Data Quality

Reliability:	
Remarks:	

References

Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1992)

Other

A2. Acute Toxicity to Fish

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt
Remarks:	Purity was 87.1% (area)

Method

Method:	Japanese Industrial Standard (JIS K 0102-1986-71)
Test type:	Flow through
GLP:	Yes
Year:	1992
Species/strain:	Oryzias latipes (Orange Killifish)
Analytical monitoring:	No; Exposure solutions, temperature, pH, dissolved oxygen
Exposure period:	96-Hour
Remarks:	A group of 10 fishes were exposed to 5 nominal concentrations(17.1-180), DMSO Control (.5mg/l)and laboratory water control

Results

Nominal concentration:	
Measured concentration:	
Endpoint value:	48 hour LC_{50} =50 mg/L
Biological observations:	
Statistical methods:	
Remarks:	

Conclusions Reliable without restrictions

Data Quality

Reliability:	
Remarks:	

References

Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1992)

Other

B. Acute Toxicity to Aquatic Invertebrates

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt

Remarks: Purity was 87.%

Method

Method:	
Test type:	OECD 202.
GLP:	Flow through, open system
Year:	Yes
Species/strain:	1984
Analytical monitoring:	Daphnid (*Daphnia magna*)
Exposure period:	No
Remarks:	21-days

Results

Nominal concentration:	
Measured concentration:	90-940 mg/L
Endpoint value:	
Reproduction	48 -hour LC_{50} 43 mg/l, 96 hour 18 mg/L, 7 days 13 mg/L, 14 days 10 mg/L ,21 days 9.7 mg/L,
Biological observations:	EC_{50} (21 days) 9.1 mg/LC_{50} (14 days) 4.4 mg/L NOEC 3.0 mg/L, LOEC 9.4
Statistical methods:	
Remarks:	95% confidence level within a range
	40 daphnids(4 replicates; 10 organisms per replicate) were exposed to 5 nominal concentrations (90-940 mg/L) control of DMSO: HCO-40 =9:1 (100mg/L) and laboratory water control

Conclusions

Reliable without restrictions

Data Quality

Reliability: This was a well-documented OECD guideline study conducted under GLP assurances.

Remarks:

References

Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1992)

Other

C. **Toxicity to Aquatic Plants**

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4- [(4- methyl-2-sulfophenyl)azo]-, calcium salt
Remarks:	Purity 87%

Method

Method:	OECD 201
Test type:	Biomass
GLP:	no
Year:	1992
Species/strain:	Selenastrum capricornutum ATCC 22662
Endpoint basis:	
Exposure period:	72 hours
Analytical procedures:	
Remarks:	

Results

Nominal concentration:	13 concentrations 1.0 to 1000 mg/L
Measured concentration:	
Endpoint value:	EC_{50} (72 hour) 190mg/L
NOEC:	5.8 mg/L ($p<.05$)
Biological observations:	
Was control response satisfactory:	Yes
Statistical Methods:	
Remarks:	

Conclusions

Data Quality

Reliability:	Reliable with restriction. This is a well documented study.
Remarks:	

References Ministry of Health and Welfare (MHW), Ministry of International Trade and Industry (MITI)

Other Environment Agency (EA), Japan (1992)

V. Toxicological Data

A. Acute Toxicity

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Barium salt
Remarks:	Purity was unknown

Method

Method:	Acute lethality; Other
Test type:	LD_{50} estimate
GLP:	No (Pre-GLP)
Year:	1968
Species/strain:	Rat/unknown
Route of exposure:	Oral gavage
Dose levels:	Unknown
Remarks:	

Results

Value:	LD_{50} = >5,000 mg/kg.
Deaths at each dose:	
Remarks:	

Conclusions Material would be considered as not toxic.

Data Quality

Reliability:	Reliable with restrictions
Remarks:	The study was conducted quite some time ago and hence many study details are missing from the report and not available. However, basic data are given and results are consistent with other data for pigments of this class.

References

Mone J.G. 1968, Federation Series on Coating Technology, Unit 9 Organic Pigments, Federation of Societies for Paint Technology, Philadelphia, PA 19107.

Other

Acute toxicity

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Calcium salt and 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(4-chloro-5- methyl-2-sulfophenyl)azo]-, Calcium salt
Remarks:	Purity was unknown

Method

Method:	
Test type:	Acute lethality; Other
GLP:	LD_{50} estimate
Year:	No (Pre-GLP)
Species/strain:	1968
Route of exposure:	Rat/unknown
Dose levels:	Oral gavage
Remarks:	Unknown

Results

Value:	
Deaths at each dose:	LD_{50} = >5,000 mg/kg.
Remarks:	

Conclusions

Material would be considered as not toxic.

Data Quality

Reliability:	
Remarks:	Reliable with restrictions The study was conducted quite some time ago and hence many study details are missing and not available. However, basic data are given and results are consistent with other data for these pigments and pigments of this class.

References

Mone J.G. 1968, Federation Series on Coating Technology, Unit 9, Organic Pigments, Federation of Societies for Paint Technology, Philadelphia, PA 19107.

Other

Repeated Dose Toxicity

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-,
Remarks:	calcium salt
	Commercial purity 98%

Method

Method:	
Test type:	OECD 422
GLP:	Combined Repeat Dose and Reproductive/ Development
Year:	Yes
Species/strain:	1992
Route of exposure:	Rat Male and Female
Duration of test:	Gavage
Exposure levels:	42 days
Sex:	0. 100, 300 or 1,000 mg/kg
Exposure period:	Male and female
Post-exposure observation	42 days including 14 days before mating
Remarks:	

Results

NOAEL (NOEL):

<100mg/kg/day, doses= 300 and 100 mg/kg/day
All animals survived to the end of the studies. No clinical findings indicative of chemical toxicity were observed; red-stained feces of exposed animals were due to contact with D & C Red No.7 and were not indicative of toxicity. The mean body weight gains and food consumption of the dosed group, in both sexes, were comparable to those in the control groups throughout the study. No biologically significant changes in hematological parameters were noted in any dosed male groups. Male rats that received 300 mg/kg or greater showed significantly decreased levels for serum calcium and phosphorus. Significant decreases in serum potassium and total cholesterol levels, and significant increases in chloride and GOT levels were also shown in the males that received 1000 mg/kg. No other significant differences in clinical parameters were observed in the dosed male groups. Male rats that received 1000 mg/kg showed a significant increase in relative kidney weights, and females that received 100 or 1000 mg/kg showed decreases in thymus weights in comparison with the controls. No other significant differences in organ weights were observed in both the males and females. At the terminal necropsy, gross pathological changes included a small thymus in 2 and 5 female rats that received 100 and 1000 mg/kg, respectively; no marked changes were noted in the dosed males. In the histopathological examinations, predominant alterations occurred in the kidney suggesting effects of D & C Red No. 7 in dosed rats. The lesions included regenerated renal tubular epithelium in male rats receiving 300 mg/kg or greater, and those with necrotic or foamy tubular epithelial cells in the dosed females. These lesions were of greater severity and/or occurred with an increased incidence in the higher dose groups. There were no histopathological changes in the sexual organs of the females that showed no evidence of the copulation, pregnancy or parturition, under the test conditions. study.

Conclusions Test substance is not significantly toxic

Data Quality
Reliability: Reliable without restriction
Remarks:

References:
Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1993)

Other

C. Genetic Toxicity - Mutation

Test Substance

Test substances: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Barium salt and 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Calcium salt

Remarks:

Method

Method: In Vitro Mutagenicity
Test type: Ames
GLP: Unknown
Year: Unknown
Species/strain: Salmonella typhimurium
Metabolic activation: Yes, barium salt (and manganese salt)
Concentration tested:
Remarks:

Results

Result: Negative
Cytotoxic concentration:
Precipitation concentration:
Genotoxic effects
With activation: Negative
Without activation: Negative
Statistical methods:
Remarks:

Conclusions

Data Quality

Reliability:
Remarks: Reliable with restrictions

References

Löser E, (1988) ETAD Report. Toxicologocal Testing of Major Colourants T201E, See also, Milvy P. & Kay K (1978), J Toxicol. Envir. Hlth. Vol. 4, p.31, and NPIRI Raw Materials Handbook, 2000

C. Genetic Toxicity - Mutation

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt

Remarks: 98% pure

Method

Method:	Japanese guideline for screening mutagenicity testing of chemicals
Test type:	Ames
GLP:	Yes
Year:	Japan (1993b)
Species/strain:	Salmonella typhimurium
Metabolic activation:	With and without
Concentration tested:	5000 ug/plate with and without activation
Remarks:	

Results

Result:	Negative in all bacterial strains with and without activation
Cytotoxic concentration:	
Precipitation concentration:	
Genotoxic effects	
With activation:	Negative
Without activation:	Negative
Statistical methods:	
Remarks:	

Conclusions

Data Quality

Reliability: Reliable without restriction Remarks:

References

Ministry of Health and Welfare (MHW),
Ministry of International Trade and Industry (MITI)
Environment Agency (EA), Japan (1993)

Other

D. **Genetic Toxicity – Chromosomal Aberrations**

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt
Remarks:	Commercial purity 98%

Method

Method:	Japanese Guideline for Screening Mutagenicity Testing of Chemicals
Test type:	Cytogenetics Assay
GLP:	Yes
Year:	1993
Species/strain:	Chinese Hamster CHL Cells
Exposure period:	
Remarks:	Activation system: S-9 fraction from the liver of Phenobarbital and 5,6-Benzoflavone induced male SD derived rats with NADPH-generating system No. replicates: 1

Results

Result:	
Genotoxic effects:	Negative
Concentration tested	Negative
Statistical methods:	0, 124, 500, 1000, or 2500 ug/plate
Remarks:	

Conclusions

Data Quality

Reliability:	Reliable without restriction
Remarks:	

References

	Ministry of Health and Welfare (MHW),
Other	Ministry of International Trade and Industry (MITI)
	Environment Agency (EA), Japan (1993)

E. Developmental Toxicity

Test Substance Description included in OECD 422 study described above

Test substance:

Remarks:

Method

Method:

GLP:

Year:

Species/strain:

Sex:

Route of exposure:

Exposure levels:

Actual doses received:

Exposure period:

Duration of test:

Remarks:

Results

Maternal toxicity

NOEL:

NOEL for teratogenicity:

NOEL for fetotoxicity:

Parental toxic responses:

Fetal toxic responses dose:

Statistical Methods:

Remarks:

Conclusions

Data Quality

Reliability:

Remarks:

References

Other

F. Toxicity to Reproduction

Test Substance

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt
Remarks:	Commercial purity 98%

Method

Method:	OECD 422
GLP:	Yes
Year:	1993a
Species/strain:	Rat
Sex:	male and female
Route of exposure:	gavage
Exposure levels:	0, 100, 300 or 1000 mg/kg
Exposure period:	males 42 days including 14 before mating/females 14 days before mating to day 3 lactation
Duration of test:	
Remarks:	

Results

Maternal toxicity NOEL:	Parental, 1000mg/kg/day
Parental toxic responses:	
Fetal toxic responses dose:	
Statistical Methods:	
Remarks:	Pertinent pregnancy and offspring parameters, e.g. mating performance, duration of gestation, pup viability, body weight and sex distribution, and gross anomalies, were determined. No treatment-related adverse effects were detected. Under the conditions of this study, NOEL for reproductive/ developmental toxicity of the rats was 1,000mg/kg/day. Method: Combined Repeated Dose and Reproductive/Developmental toxicity Screening Test

Conclusions

Data Quality

Reliability:	Reliable without restriction
Remarks:	

References Ministry of Health and Welfare (MHW), Ministry of International Trade and Industry (MITI)

Other Environment Agency (EA), Japan (1993) MHW

Acute toxicity

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Barium salt **and** 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Calcium salt
Remarks:	

Method

Method:	Irritation to the rabbit eye
Test type:	eye irritation
GLP:	unknown
Year:	1972
Species/strain:	rabbitt
Route of exposure:	
Dose levels:	
Remarks:	

Results

Value:	negative
Deaths at each dose:	
Remarks:	

Conclusions

Data Quality

Reliability:	unassignable
Remarks:	

References **Company data**

Other

Acute toxicity

Test substance:	2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Barium salt and 2-Naphthalenecarboxylic acid, 3-hydroxy-4-(5-chloro-4- methyl-2-sulfophenyl)azo]-, Calcium salt
Remarks:	

Method

Method:	Skin irritation to the rabbit
Test type:	Skin irritation
GLP:	unknown
Year:	1972
Species/strain:	rabbit
Route of exposure:	
Dose levels:	
Remarks:	

Results

Value:	negative
Deaths at each dose:	
Remarks:	

Conclusions

Data Quality

Reliability:	unassignable
Remarks:	

References

Company data, A subchronic, 18 month dermal toxicity study for C.I. Pigment Red 57 has also been reported. An aqueous suspension of pigment was applied to 50 male and 50 female mice twice weekly for 18 months. Survival was unaffected and there were no clear effects on the gross or microscopic appearance of a range of tissues. See BIBRA Report (1993)

Other

Chronic Dose Toxicity

Test Substance

Test substance: 2-Naphthalenecarboxylic acid, 3-hydroxy-4-[(4- methyl-2-sulfophenyl)azo]-, calcium salt

Remarks:

Method

Method: Chronic Toxicity

Test type: Repeated oral dose

GLP: unknown

Year: Reported in (1993)

Species/strain: Rat

Route of exposure: Oral gavage

Duration of test: two years

Exposure levels: .05, .3, and 2%

Sex: 70 Males and 70 Females (The offspring of rats which had been tested at the same levels for 60 days prior to mating and throughout pregnancy and lactation)

Exposure period:

Post-exposure observation period:

Remarks:

Results

NOAEL (NOEL): NOAEL 150 mg/kg/bw/day

Conclusions At the end of the study, the weights and gross appearance of the major organs were unaffected, except in the high dose male rats which showed organ weight variations relative to their reduced body weight. Microscopic examination of the major tissues (limited to the control and high dose animals) revealed an increased incidence of kidney changes in both males and females. When pathologists from the U.S. Food and Drug administration subsequently examined tissue sections from the kidneys of all treated rats, they concluded that the test substance exacerbated a spontaneous kidney disease in aged rats (chronic progressive nephrosis) in the mid- and high-dose males and in high dose females. An acceleration of testicular changes (degeneration of testicular tubules), common in aging rats, was also reported in high dose males, but the increased incidence was of no statistical significance.

Data Quality

Reliability: unassignable

Remarks:

References Reported in detail in the BIBRA (1993) Profile for Lithol rubine. See also, Opinion of the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers (a scientific advisory body to the European Commission) Concerning Pigment Red 57, adopted May 25, 2004.

Chronic toxicity Notes: Chronic studies using mice and dogs are also reported, the lowest NOEAL is at 150 mg/kg/bw/day, study reported above

Other

Other

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